

UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 10/788,489 Confirmation No. 9027

Applicant : Serge CARILLO, et al.

Filed : March 1, 2004

Title : METHOD OF CANCER TREATMENT BY P53 PROTEIN CONTROL

TC/AU : 1633

Examiner : Scott LONG

Docket No. : ST94037B / 80375.0033

Customer No. : 55962

MAIL STOP PETITION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION FROM REFUSAL TO ENTER AMENDMENT OR WITHDRAWAL OF FINALITY UNDER 37 C.F.R. § 1.181(a)

Sir:

In response to the Advisory Action dated November 26, 2008, and reply to Applicants' request for withdrawal of finality, Applicants petition the Director for review of the Examiner's actions and submit the following remarks in support. In particular, Applicants respectfully request entry of an amendment in the above-identified patent application or withdrawal of finality of the Office Action. The required fee is attached.

I. INTRODUCTION

Applicants submit that the Examiner's refusal to enter an amendment to claim 1 in the above-mentioned case was improper for at least three reasons. First, Applicants contend that the Examiner improperly made a second action containing a new ground of rejection final. Because this action was incorrectly made final, Applicants were not afforded an appropriate opportunity to reply and amend their claims. Second, Applicants assert that, even if the second action was properly made final, the proposed amendment to claim 1 presents the claim in a better form for appeal. Third, Applicants contend that the Examiner's stated reasons for refusing to enter the amendment are particularly unpersuasive in light of the prosecution history and the searches that the Examiner conducted early in prosecution.

Accordingly, Applicants respectfully request that the proposed amendment to claim 1 be entered.

II. STATEMENT OF FACTS INVOLVED

Applicants filed the instant application on March 1, 2004. The application was specifically directed to a method for detecting an inhibitor of a protease that degrades p53. As filed, the application contained eight claims, with claim 1 being in independent form. The text of originally-filed claim 1 is included below:

1. A method for detecting an inhibitor of p53 protein degradation comprising providing a cell extract containing one or more p53 proteins and one or more proteases, administering an inhibitor of calpain protease activity, and measuring p53 and p53 protein fragments.

In initially examining the claims, the Examiner conducted several searches for relevant prior art. Significantly, the Examiner specifically utilized the following search terms in his earliest searches "p53 and inhibit\$4 and (cell with extract\$4)." See Examiner's Search Strategy and Notes (dated August 10, 2007). After conducting these searches, the Examiner proceeded to reject claim 1 under 35 U.S.C. §§ 102 and 103. According to the Examiner, claim 1 was anticipated by Ramsby (Electrophoresis, Feb 1994, 15(2): 265-77), which discusses the use of EDTA. Moreover, the Examiner

rejected claim 1 as obvious over the combination of Ramsby and Asada (J. Enzym. Inhib. 1989, 3(1): 49-56). See First Office Action at pages 7-11.

Applicants proceeded to amend claim 1 to recite a "peptide or protein" inhibitor of calpain protease activity. In the subsequent action on the merits, the Examiner withdrew the 35 U.S.C. §§ 102 and 103 rejections in light of Applicants' persuasive arguments. See Second Office Action at pg 5. However, the Examiner introduced a new ground of rejection. See Second Office Action at pages 6-10. Specifically, the Examiner rejected all claims under 35 U.S.C. § 103 over five references that allegedly disclosed the following "limitations:" (1) calpastatin's role as a calpain inhibitor (2) use of calpastatin derivatives (3) use of other calpain inhibitors (4) p53's role in apoptosis (5) differential detergent fractionation of p53 and (6) use of electrophoresis. Despite the fact that these "limitations" were present in the original, unamended claims, the Examiner made the action a Final Office Action.

On October 30, 2008, Applicants filed a response requesting reconsideration and withdrawal of the finality of the second Office Action. See Response to Second Office Action at pages 3-4. Moreover, Applicants presented the following amendment:

1. A method for detecting an inhibitor of p53 protein degradation comprising providing a cell extract containing one or more p53 proteins and one or more proteases, administering a peptide or protein inhibitor of calpain protease activity to the cell extract, and measuring p53 protein and p53 protein fragments.

In their remarks, Applicants explained that this amendment merely clarified what the skilled artisan would already understand about the claim. See Response to Second Office Action at pg 6.

Nevertheless, the Examiner issued an Advisory Action on November 26, 2008. The Examiner refused to enter the amendment, asserting that the amendment would require "further search and consideration." See Advisory Action at pg 2. Moreover, the Examiner refused to withdraw the finality of the second action, explaining that the language of the claims prior to the initial amendment was "sufficiently broad to allow the examiner to apply art rejections which read on the originally filed claims, whereas the amended claims (filed 2/19/2008) could no longer be viewed as anticipatory or obvious over the cited art." See *id.* Applicants now timely file this Petition.

III. POINTS TO BE REVIEWED

A. The Second Action Was Improperly Made Final.

In making the second action final despite its inclusion of a new ground of rejection wholly unrelated to Applicants' amendment of the claims, the Examiner disregarded the basic precept that an action containing new grounds of rejection can only be made final in very limited circumstances. Indeed, a second action containing new grounds of rejection cannot be made final unless the new grounds of rejection are "necessitated by applicant's amendment of the claims" or "based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p)." MPEP § 706.07(a).

Contrary to the Examiner's assertion, the new grounds of rejection introduced in the second final action were not "necessitated by applicant's amendment of the claims." Rather, the rejection could have been made in the first Office Action, affording the Applicants an appropriate opportunity to reply. Indeed, the Henkart (US 5,607,831), Haake (J. Invest. Dermatol, 1993; 101: 107-112), Squier (Journal of Cellular Physiology, May 1994; 159(2): 229-237), Maki (The Journal of Biological Chemistry, Nov. 15, 1989; 264(32): 18866-18869), and Ramsby (Electrophoresis, Feb. 1994; 15(2): 265-67) references cited in the second action are said by the Examiner to allegedly disclose the following "limitations": (1) calpastatin's role as a calpain inhibitor (Henkart, Squier, Maki) (2) use of calpastatin derivatives (Henkart, Maki) (3) use of other calpain inhibitors (Squier) (4) p53's role in apoptosis (Haake) (5) differential detergent fractionation of p53 (Ramsby) (6) use of electrophoresis (Henkart, Squier, Ramsby).

All of these alleged "limitations" were present in the original, unamended claims. More specifically, claim 2 has always disclosed that the inhibitor is a calpastatin, meaning that the Henkart, Squier, and Maki references could have been cited in the initial Office Action. Additionally, independent claim 1 has always disclosed "providing a cell extract containing one or more p53 proteins," meaning that Haake and Ramsby could have been cited in the initial Office Action.

Because the second action was improperly made final, Applicants were not afforded a proper opportunity to reply and amend their claims. Applicants accordingly

respectfully request reconsideration and withdrawal of the finality of the second action, and entry of their proposed claim amendment.

B. The Proposed Amendment Presents Claim 1 in Better Form for Consideration on Appeal.

Even if the second action was properly made final, the proposed amendment comports with the specific regulations governing when an amendment after final may be entered. Indeed, the MPEP provides that “[a]ny amendment that will place the application either in condition for allowance or in better form for appeal may be entered.” See MPEP § 714.12.

The proposed amendment falls precisely within this standard. Indeed, the amendment merely clarifies what the skilled artisan would already understand: that the inhibitor of calpain protease activity is being administered to the cell extract containing one or more p53 proteins and one or more proteases. This is the only sensible reading given that an enzyme inhibitor “interact[s] in some way with [an] *enzyme* to prevent it from working in the normal manner.” Charles E. Ophardt, *Enzyme Inhibitors*, Virtual Chembook (2003) (emphasis added) (see Response dated October 30, 2008).

Moreover, the Examiner tacitly admits that claim 1 is in a better form for appeal. Specifically, in the Advisory Action, the Examiner emphasized that, prior to the first amendment, “the nature of the claim language . . . was sufficiently broad to allow the examiner to apply art rejections which read on the originally filed claims, whereas the amended claims (filed 2/19/2008) *could no longer be viewed as anticipatory or obvious over the cited art.*” See Advisory Action at pg 2 (emphasis added). If the amended claims are no longer viewed as anticipated or obvious in view of the cited art, the application would seem to be in a better form for appeal. Accordingly, Applicants respectfully submit that the proposed amendment presents claim 1 in a better form for consideration on appeal and simplifies the issues on appeal.

C. The Examiner’s Stated Reasons for Refusing to Enter the Amendment are Improper.

Contrary to the Examiner’s reasoning, entry of this amendment would not necessitate a new search. According to the Examiner, a new search would be required

because the amendment would “further limit the claims.” See Advisory Action at pg 2. The Examiner’s argument is flawed for at least two reasons.

First, the Examiner implicitly acknowledged throughout prosecution that the claim contained the very “limitation” that he is asserting requires a new search. Indeed, in his first Office action, the Examiner specifically stated that “Ramsby et al. teach . . . use of EDTA which is ‘an effective inhibitor of the calcium-activated proteases, calpains I and II.’” See First Office Action at pg 7. Moreover, the Examiner provided that “Ramsby et al. teach that their method ‘is applicable to use with limited amounts of biomaterial and with other cell types or culture systems’ . . . inferring *that it is obvious to use their system with any cell extract*, including tumor cell extracts.” See First Office Action at pg 9 (emphasis added). The highlighted language confirms that the Examiner understood throughout prosecution that the peptide or protein inhibitor of calpain protease activity was specifically administered to the cell extract. Thus, it is particularly incongruous for the Examiner to assert that this amendment would somehow require a new search when he proceeded throughout prosecution as if this language was already in the claim.

Second, the Examiner has already searched for the “limitation” he asserts requires a new search. Indeed, as evidenced by initial search strategy and results, the Examiner initially utilized the following search query in examining the application: “p53 and inhibit\$4 and (cell with extract\$4).” See Examiner’s Search Strategy and Notes (dated August 10, 2007). Consequently, the Examiner’s argument that incorporating this “limitation” into claim 1 would require a “new search” is specious given that he has already searched for this very term.

Accordingly, Applicants respectfully submit that the proposed amendment to claim 1 should be entered.

IV. ACTION REQUESTED

For at least the foregoing reasons, Applicants respectfully submit that the proposed amendment to claim 1 should be entered or that the finality of the Office Action be withdrawn.

CONCLUSION

Applicants respectfully request entry of the proposed amendment and timely notification of allowability. If there are any additional fees due with the filing of this document, or any attached document, including fees for the net addition of claims, applicants respectfully request that any and all fees be charged to Deposit Account No. 50-1129. If any extension of time request or any petition is required for the entry of this paper or any of the accompanying papers, applicants hereby petition or request the extension necessary. The undersigned authorizes any fee payment from Deposit Account No. 50-1129. Furthermore, if additional extensions of time are required to enter this amendment beyond any provided for, applicants respectfully request an extension and the undersigned hereby authorizes that any fees be taken from Deposit Account No. 50-1129, referencing Attorney Docket No. 80375.0033.

Respectfully submitted,

WILEY REIN LLP

Date: January 26, 2009

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